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Tremor and Other Hyperkinetic Movements

Brief Reports

Voice Handicap in Essential Tremor: A Comparison with Normal Controls and Parkinson's Disease

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Abstract

Background: Although voice tremor is one of the most commonly noted clinical features of essential tremor (ET), there are nearly no published data on the handicap associated with it.

Methods: The Voice Handicap Index (VHI) was self-administered by participants enrolled in a research study at Columbia University Medical Center. The VHI quantifies patients' perceptions of handicap due to voice difficulties. Data from 98 ET cases were compared with data from 100 controls and 85 patients with another movement disorder (Parkinson's disease, PD).

Results: Voice tremor was present on examination in 25 (25.5%) ET cases; 12 had mild voice tremor ($ET_{Mild\ VT}$) and 13 had marked voice tremor ($ET_{Marked\ VT}$). VHI scores were higher in ET cases than controls ($p=0.02$). VHI scores among $ET_{Marked\ VT}$ were similar to those of PD cases; both were significantly higher than controls ($p<0.001$). The three VHI subscale scores (physical, functional, emotional) were highest in $ET_{Marked\ VT}$, with values that were similar to those observed in PD.

Discussion: The voice handicap associated with ET had multiple (i.e., physical, functional, and emotional) dimensions. Moreover, ET cases with marked voice tremor on examination had a level of self-reported voice handicap that was similar to that observed in patients with PD.

Keywords: Essential tremor, voice tremor, handicap, Voice Handicap Index, Parkinson's disease, function, clinical

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Introduction

A common feature of many movement disorders is that, through a variety of mechanisms, they may involve the voice, thereby producing a range of problems for those with the disease, and affecting the ability to communicate. Voice tremor is a well-described phenomenon in patients with essential tremor (ET),[1–4] occurring in as many as 40% of cases in some population-based studies[5] as well as in some referral settings.[6] Voice tremor in ET is the focus of treatment efforts with medications,[7,8] botulinum toxin injections,[9,10] and, in severe and refractory cases, deep brain stimulation surgery.[11,12] As a "midline tremor," voice tremor is more resistant to treatment efforts, and achieving satisfactory therapeutic results may be challenging. Although voice tremor is one of the items listed in quality of life scales for ET,[13] there are nearly no published data on the handicap and disability associated with voice tremor in ET. What are the psychosocial consequences of voice tremor in ET?

The Voice Handicap Index (VHI) was developed to measure patients' perception of disability due to their voice disorder.[14] It broadly assesses the functional, physical, and emotional aspects of voice disorders. With one exception, it has not been applied to ET patients.[1] This study had several aims. First, using the VHI, we quantified ET patients' handicap due to their voice disorder using two reference points: normal controls and patients with Parkinson's disease

(PD). Second, using the VHI, we assessed the functional, physical, and emotional aspects of the voice disorder in ET. Third, as ET patients with voice tremor do not represent a single homogeneous group, we aimed to further refine our assessment of voice-related handicap in ET by sorting ET patients into two groups (mild tremor vs. marked tremor on examination).

Methods

Study sample

Participants were enrolled in a clinical–epidemiological research study at Columbia University Medical Center (CUMC).[15–17] The majority of the ET cases were patients at the Center for Parkinson's Disease and Other Movement Disorders (CPD) at the Neurological Institute of New York (CUMC). PD cases were also patients at the CPD.[15–17] Using the Neurological Institute's computerized billing database, ET and PD cases were selected randomly from a list of patients seen over the past 5 years. Normal controls were selected from the same source population as ET cases (i.e., the same set of zip codes).[17] They were recruited using random-digit telephone dialing and frequency matched by age, gender, and race to ET cases. The majority of controls also received their health care at the same medical center (CUMC) as the ET cases in various outpatient departments (e.g., medicine, surgery).[17] All cases and controls were screened using the Telephone Interview for Cognitive Status,[18] and those who showed signs of cognitive impairment (score <31) were excluded.

Diagnoses

Each ET or PD case had been diagnosed by a CPD neurologist who specialized in movement disorders.[17] PD was diagnosed when two or more cardinal features of parkinsonism were present in the absence of other possible causes (e.g., stroke, atypical parkinsonian syndromes, medication). All PD diagnoses were also reconfirmed based on clinical chart review by a senior movement disorder neurologist (E.D.L.).[17] ET was diagnosed when moderate or greater amplitude action tremor was present in the arms or head tremor was present in the absence of another known cause of tremor (e.g., medications, PD, or dystonia). Given the common misdiagnosis of ET in published reports,[19] ET diagnoses were further reconfirmed. After videotaped examination (see below), ET diagnoses were reconfirmed in each case using published diagnostic criteria (moderate or greater amplitude kinetic tremor on three or more tests or head tremor).[17,20,21]

There were 100 ET cases, 100 controls, and 90 PD cases. We excluded two ET cases and five PD cases with incomplete information, resulting in a final sample of 98 ET cases, 100 controls, and 85 PD cases.

Study procedure

Upon enrollment, all participants gave written informed consent approved by the CUMC Institutional Review Board. Participants were evaluated in person by a trained tester who administered structured clinical questionnaires that elicited demographic and clinical information.[17]

The VHI[14] was developed to quantify patients' perceptions of disability due to voice difficulties. The VHI has been shown to have test–retest reliability and construct validity, and has also been shown to be sensitive for a wide variety of voice disorders.[14,22] This self-administered questionnaire consists of 30 questions; the patient responds according to the appropriateness of each item (0=none to 4=always). These 30 questions are equally distributed over three domains: functional, physical, and emotional aspects of voice disorders. The functional subscale assesses the impact of a person's voice disorder on his or her daily activities (e.g., "people ask me to repeat myself when speaking face-to-face"). The emotional subscale assesses the patient's affective responses to a voice disorder (e.g., "My voice problem upsets me"). The items in the physical subscale assess the patient's self-perceptions of laryngeal discomfort and the voice output characteristics (e.g., "The clarity of my voice is unpredictable"). The VHI was designed to assess all types of voice disorders, even those encountered by tracheoesophageal speakers. The VHI is scored from 0 to 120 (maximum perceived disability due to voice difficulties), and each of the three subscores is scored from 0 to 40 (maximum perceived disability).

Medical co-morbidity was assessed using the Cumulative Illness Rating Scale (CIRS), in which the severity of medical problems (0 [none] to 3 [severe]) was rated in 14 body systems (e.g., cardiac, respiratory, renal) and a CIRS score was assigned (range 0–42 [maximal co-morbidity]) to each subject.[23] A Hoehn and Yahr score was assigned to each PD case.[24]

The Center for Epidemiological Studies Depression Scale (CESD-10), a self-report, 10-item screening questionnaire for depressive symptoms (range 0–30 [greater depressive symptoms])[25] was added. The CESD-10 has been shown to have good reliability, and excellent sensitivity and specificity using a diagnosis of Major Depressive Disorder as diagnosed using the *Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders*, Third Edition, Revised, as the gold standard.[26,27]

Each ET case also underwent a videotaped neurological examination, which included an assessment of postural tremor, five tests of kinetic tremor, and speech. A senior movement disorders neurologist (E.D.L.) reviewed all videotaped examinations, and the severity of postural and kinetic tremors were rated (0–3), resulting in a total tremor score (range 0–36 [maximum]), a measure of the severity of the action tremor.[28] Voice tremor was assessed during sustained phonation, conversational speech, and while reading a prepared passage. The overall severity of the voice tremor was rated as absent, mild, moderate, or severe. ET cases were stratified into those with no voice tremor on examination, those with mild voice tremor ($ET_{Mild\ VT}$), and those with marked (moderate or severe) voice tremor ($ET_{Marked\ VT}$).

Statistical analyses

Statistical analyses were performed in SPSS (version 19.0; Chicago, Illinois). Demographic and clinical characteristics were compared

using chi-square tests and Student's t-tests. The VHI scores were not normally distributed (Kolmogorov–Smirnov $p<0.001$); therefore, non-parametric tests (Kruskal–Wallis test, Mann–Whitney test, Spearman's rho) were used when assessing this variable. For our main analysis, VHI scores were compared across the three diagnostic groups (ET, controls, PD) using a Kruskal–Wallis test; when a group difference was detected, Mann–Whitney tests were further employed to identify specific differences (i.e., ET vs. controls, PD vs. controls, ET vs. PD). In addition, we assessed VHI scores in ET subgroups (ET without voice tremor, $ET_{Mild\ VT}$, $ET_{Marked\ VT}$) relative to controls and PD cases. A CESD-10 cut-off score ≥ 20 has been recommended for depression;[29] in one analysis, we excluded individuals with a score ≥ 20, and in a second analysis, we further excluded individuals with mild depressive symptoms (CESD-10 ≥ 10).[25,30]

Results

Demographic and clinical characteristics of study groups

The three groups (ET, PD, controls) were similar in terms of age, education, and CIRS scores (Table 1). As expected, the majority of PD cases were men, more PD than ET cases were taking daily medication for their disease, and disease duration was shorter in PD than ET cases (Table 1). The CESD-10 score differed across groups, with controls having the lowest scores and PD cases having the highest scores (Table 1). For PD cases, 80 (94.1%) were Hoehn and Yahr stage I or II.

Correlates of VHI score

In controls, VHI was not associated with age (Spearman's $r=-0.001$, $p=0.99$), years of education (Spearman's $r=-0.02$, $p=0.82$), gender (Mann–Whitney $z=0.77$, $p=0.44$), CESD-10 score (Spearman's $r=0.07$, $p=0.47$) or CIRS score ($p=0.04$, $p=0.68$).

There was a correlation between VHI score and disease duration in ET (Spearman's $r=0.22$, $p=0.04$) and disease duration in PD (Spearman's $r=0.29$, $p=0.016$), and a correlation between VHI score and total tremor score in ET (Spearman's $r=0.37$, $p=0.001$). Among ET cases and PD cases, there was a correlation between VHI scores and CESD-10 scores (Spearman's $r=0.34$ [$p<0.001$], and Spearman's $r=0.40$ [$p<0.001$], respectively).

VHI in ET cases vs. other study groups

The VHI score differed across the three groups (ET, PD, control, Kruskal–Wallis test=51.5, $p < 0.001$); it was higher in ET cases than controls ($p=0.02$), and higher in PD cases than controls ($p < 0.001$) (Table 2). PD cases had higher VHI scores than ET cases (Mann–Whitney test=4.45, $p <0.001$) (Table 2).

VHI subscores (functional, physical, and emotional)

Each of the three VHI subscale scores differed across the three groups (ET, PD, control, each $p<0.001$ in a Kruskal–Wallis test). The VHI emotional subscale score ($p=0.001$) and VHI physical subscale score ($p=0.003$) were higher in ET cases than controls; the VHI functional subscale score was marginally higher in ET cases than controls ($p=0.10$) (Table 2). Each of the three VHI subscale scores was higher in PD cases than controls (each $p<0.001$) (Table 2).

ET cases had higher scores than controls in 24 of the 30 VHI items (all 24 $p<0.05$ in Mann–Whitney tests), including 9 of the 10 VHI emotional subscale items, 8 of the 10 VHI physical subscale items, and

Table 1. Demographic and Clinical Characteristics of Study Subjects

	ET	ET (no voice tremor)	ET (mild voice tremor)	ET (marked voice tremor)	PD	Control
N	98	73	12	13	85	100
Age (years)	70.2 ± 12.5	68.4 ± 12.3	70.8 ± 13.2	79.9 ± 8.3	69.0 ± 8.2	72.0 ± 9.7
Female gender**	49 (50.0)	30 (41.1)	8 (66.7)	11 (84.6)	34 (40.0)	64 (64.0)
Education (years)	16.1 ± 2.5	16.1 ± 2.6	16.8 ± 1.5	15.0 ± 2.4	16.0 ± 3.1	16.2 ± 2.5
Duration of disease (years)***	30.3 ± 17.6	28.8 ± 16.2	29.0 ± 20.5	39.6 ± 20.5	9.9 ± 10.1	NA
Takes medication for ET or PD***	55 (56.1%)	41 (56.2%)	6 (50.0%)	8 (61.5%)	85 (100)	NA
Total tremor score	20.7 ± 5.6	20.0 ± 5.7	21.9 ± 3.4	23.7 ± 6.0	NA	NA
CIRS score	6.9 ± 3.4	6.7 ± 3.4	7.5 ± 3.5	7.4 ± 3.6	6.9 ± 3.3	6.5 ± 3.5
CESD-10***	8.3 ± 6.3	8.0 ± 6.0	10.7 ± 7.5	8.1 ± 6.8	10.0 ± 5.9	5.5 ± 3.7

Values are mean ± standard deviation or number (percentage).
*$p<0.05$, **$p<0.01$, ***$p<0.001$ comparing three groups (ET, PD, and controls) or two groups (ET vs. PD).
Abbreviations: CESD-10, Center for Epidemiological Studies Depression Scale; CIRS, Cumulative Illness Rating Scale score; ET, essential tremor; NA, not applicable; PD, Parkinson's disease.

Table 2. VHI Scores in Study Subjects

	ET (All ET)	ET (no voice tremor)	ET (mild voice tremor)	ET (marked voice tremor)	PD	Control
N	98	73	12	13	85	100
VHI***	13.1 ± 22.2	10.1 ± 19.3	13.3 ± 18.8	30.0 ± 32.8	24.6 ± 23.2	3.6 ± 5.2
	3.0 (0–103)	2.0 (0–103)	2.5 (0–51)	16.0 (0–96)	18.0 (0–90)	1.0 (0–31)
	p=0.02[1]	p=0.21[1]	p=0.32[1]	p<0.001[1]	p<0.001[1]	
VHI functional Subscale score***	4.4 ± 7.3	3.3 ± 6.3	4.8 ± 6.3	10.1 ± 10.9	8.5 ± 7.9	1.8 ± 2.4
	0.5 (0–32)	0.0 (0–18)	1.5 (0–18)	7.0 (0–32)	7.0 (0–32)	0.0 (0–11)
	p=0.10[1]	p=0.55[1]	p=0.24[1]	p=0.002[1]	p<0.001[1]	
VHI emotional Subscale score***	3.9 ± 8.2	2.8 ± 7.1	4.9 ± 7.9	9.0 ± 11.8	6.4 ± 8.0	0.5 ± 1.5
	0.0 (0–37)	0.0 (0–37)	0.0 (0–21)	2.0 (0–32)	2.0 (0–31)	0.0 (0–10)
	p=0.001[1]	p=0.03[1]	p=0.007[1]	p<0.001[1]	p<0.001[1]	
VHI physical Subscale score***	4.8 ± 7.5	4.0 ± 6.6	3.6 ± 5.6	10.9 ± 10.8	9.8 ± 8.5	1.4 ± 2.1
	2.0 (0–34)	1.0 (0–34)	0.5 (0–15)	7.0 (0–32)	8.0 (0–29)	0.0 (0–10)
	p=0.003[1]	p=0.03[1]	p=0.43[1]	p<0.001[1]	p <0.001[1]	

Values are mean ± standard deviation, median (minimum - maximum).
*p<0.05, **p<0.01, ***p<0.001 comparing three groups (ET, PD and controls) using a Kruskal–Wallis test.
[1]Mann–Whitney test compared with controls.
Abbreviations: ET, essential tremor; PD, Parkinson's disease; VHI, Voice Handicap Index.

7 of the 10 VHI functional subscale items. PD cases had higher scores than controls in 29 of 30 items (all 29 p<0.05 in Mann–Whitney tests).

VHI in ET subgroups

Voice tremor was present on examination in 25 (25.5%) of 98 ET cases, including 12 (12.2%) $ET_{Mild\ VT}$ and 13 (13.3%) $ET_{Marked\ VT}$. The VHI scores among $ET_{Marked\ VT}$ were similar to those of PD cases; both were significantly higher than controls (p<0.001, Table 2). The three VHI subscale scores were highest in $ET_{Marked\ VT}$, with values that were similar to or higher than those seen in PD (Table 2).

In ET cases, VHI scores were marginally correlated with age (Spearman's r=0.19, p=0.06), and ET subgroups differed with respect to age (ET cases without voice tremor were younger than $ET_{Marked\ VT}$ [Tukey's post hoc test p = 0.005]). To explore the possible confounding effects of age, we stratified ET cases based on their median age (72 years), and in each age stratum, the VHI score was higher in $ET_{Marked\ VT}$ than in ET cases without voice tremor (data not shown), indicating that age was not an important source of confounding.

$ET_{Marked\ VT}$ had higher scores than controls in 26 of 30 VHI items (all 26 p<0.05 in Mann–Whitney tests). $ET_{Marked\ VT}$ differed from PD cases in 0 of 30 items (none of the 30 p < 0.05 in Mann–Whitney tests).

ET cases without voice tremor had higher scores than controls in 16 of 30 items (including 8 of the 10 VHI emotional subscale items, 6 of the 10 VHI physical subscale items, and 2 of the 10 VHI functional subscale items). In an analysis in which we excluded seven ET cases and five controls with a CESD-10 score ⩾20, ET cases without voice tremor had higher scores than controls in 14 of 30 items, but when we excluded 25 ET cases and 19 controls with CESD ⩾10, ET cases without voice tremor had higher scores than controls in only 4 of 30 items. By comparison, ET cases with voice tremor differed from controls in 20 of 30 items (excluding those with CESD-10 score ⩾20) and 11 of 30 items (excluding those with CESD-10 score ⩾10).

ET cases (no VT, mild VT, marked VT) did not differ from one another in terms of the proportion who were taking ET medication (Table 1, chi-square=0.34, p=0.85). Seven (7.1%) ET cases had surgery for ET (five deep brain stimulation and two other); when these seven were excluded, the observed differences in VHI scores remained.

Discussion

What is the biopsychosocial impact of a voice disorder? We used a patient-based, voice-specific outcome measure to assess the impact that voice tremor has on daily voice-related functions in ET. The voice handicap that was associated with ET was multi- rather than unidimensional, including physical, functional, and emotional aspects. Moreover, VHI subscores were particularly high in ET cases with marked voice tremor on examination, and approached levels seen in patients with PD. A range of speech problems is well known to occur in

patients with PD, including problems with volume, intonation, and verbal fluency.[31] These problems, which may be quite severe, are the focus of a range of therapeutic efforts.[32,33]

While there has been some study of the impact of voice tremor in normal aging[34] and other settings,[35] there has been surprisingly little formal study of the handicap and disability associated with voice tremor in ET, despite the high prevalence of voice tremor among ET patients. One prior study used the VHI in 34 ET cases referred to an academic laryngology practice; VHI scores were high (71 ± 28) in that highly-select, specialty setting.[1] We are not aware of other studies of voice handicap in ET.

Of interest is that even ET cases without voice tremor differed from controls in approximately one-half (16 of 30) of the VHI items. As the VHI is a self-report instrument, some of the VHI items might be proxies for depression. In an analysis in which we excluded individuals with depression (CESD-10 score $\geq$20), ET cases without voice tremor had higher scores than controls in 14 of 30 VHI items, but when we excluded 25 ET cases and 19 controls with a CESD-10 score $\geq$10 (i.e., mild depressive symptoms or depression), ET cases without voice tremor had higher scores than controls in only 4 of 30 items.

This study had limitations. The number of ET cases with voice tremor was modest (n=25); despite this, we were able to detect significant differences in most of our main analyses.

In summary, the voice handicap associated with ET had multiple (i.e., physical, functional, and emotional) dimensions. Moreover, ET cases with marked voice tremor on examination had a level of self-reported voice handicap that was similar to that observed in patients with PD.

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